

**FACSIMILE TRANSMISSION SHEET**

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**TO: Examiner Thurman Michael Wheeler**

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**FROM: Sean Mellino (D. Peter Hochberg Co., L.P.A.)**

**DATE: September 16, 2011**

**TOTAL PAGES: 6**

**MESSAGE:**

Re: App. No. 10/590,601 (Our ref. RO4304US.RCE (#90568))

Dear Examiner Wheeler:

Enclosed is a proposed set of amended claims for review in anticipation of the telephone interview on September 21, 2011.

Kind regards,

*Sean Mellino*

\* \* \* \* \*

**CERTIFICATE OF MAILING**

I hereby certify that this document is being deposited with the United States Postal Service as First Class mail in an envelope addressed: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on the date noted below:

Date: \_\_\_\_\_

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Sean Mellino**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant : Sabine Balthasar, et al.  
Serial No. : 10/590,601 (Conf. No. 8967)  
Filing Date : August 24, 2006  
Examiner : Thurman Michael Wheeler  
Group Art Unit : 1619  
Title : Carrier System in the Form of Protein-Based Nanoparticles  
for the Cell-Specific Enrichment of Pharmaceutically  
Active Substances  
Attorney File : RO4304US.RCE (#90568)

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia, 22313-1450

**Response to the Final Office Action Issued July 15, 2011**

Dear Sir:

In response to the Final Office action issued July 15, 2011, please amend the  
above identified application without prejudice as follows:

**In the Claims:**

1. (currently amended) A carrier system for the cell-specific, intracellular enrichment of at least one pharmacologically active substance, wherein said carrier system is present in the form of protein-based nanoparticles to which biotinylated antibodies are bound, wherein said nanoparticles are based on at least one protein selected from the group consisting of gelatine and serum albumin, and said biotinylated antibodies are bound by forming a stable avidin-biotin complex with fluorescein-conjugated deglycosylated avidin which is covalently bound to the nanoparticles by bifunctional spacer molecules which are attached to reactive groups present on the surface of the nanoparticles; and wherein said antibodies enable a cell-specific attachment and cellular absorption of the nanoparticles.
2. (previously presented) The carrier system according to claim 1, wherein the reactive group is selected from the group consisting of an amino group, a thiol group, a carboxyl group and an avidin derivative.
3. (canceled)
4. (previously presented) The carrier system according to claim 1, wherein the antibody is a monoclonal antibody.
5. (previously presented) The carrier system according to claim 1, wherein said carrier system additionally comprises a pharmaceutically active substance that is bound to the carrier system by the reactive groups by a method selected from the group consisting of adsorption, incorporation, covalent bonds and complexing bonds.
6. (withdrawn) Use of a carrier system according to claim 1 for producing a medicament for enrichment of a pharmaceutically active substance to/in specific cells.

7. (withdrawn) A method for producing a carrier system in the form of protein-based nanoparticles for the cell-specific enrichment of at least one pharmacologically active substance, wherein said method comprises the following steps:

desolvating an aqueous protein solution to form nanoparticles;

stabilising the nanoparticles formed by the desolvation step by crosslinking;

converting part of the functional groups on the surface of the stabilised

nanoparticles to reactive thiol groups;

covalently attaching functional proteins by bifunctional spacer molecules;

if required, biotinylating the antibody;

loading the functional-protein-modified nanoparticles with the biotinylated antibody; and

loading the functional-protein -modified nanoparticles with a biotinylated and pharmaceutically or biologically active substance.

8. (withdrawn) The method according to claim 7, wherein the protein base is selected from the group consisting of gelatine and serum albumin.

9. (withdrawn) The method according to claim 7, wherein the desolvation step is carried out by a method selected from the group consisting of stirring and adding a water-miscible non-solvent for proteins and by salting-out.

10. (withdrawn) The method according to claim 9, wherein the water-miscible non-solvent for proteins is selected from the group consisting of ethanol, methanol, isopropanol and acetone.

11. (withdrawn) The method according to claim 7, wherein said step of stabilising the nanoparticles is achieved by utilising at least one method selected from the group consisting of thermal processes, bifunctional aldehydes and formaldehyde.
12. (withdrawn) The method according to claim 11, wherein said bifunctional aldehyde is glutaraldehyde.
13. (withdrawn) The method according to claim 7, further comprising the step of using a substance as the thiol group-modifying agent that is selected from the group consisting of 2-iminothiolane, a combination of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide and cysteine, a combination of 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide and cystaminium dichloride and dithiotreitol.
14. (withdrawn) The method according to claim 7, further comprising the step of using a substance as a bifunctional spacer molecule that is selected from the group consisting of m-maleimidobenzoyl-N-hydroxysulfosuccinimide ester, sulfosuccinimidyl-4-[N-maleimido-methyl]cyclohexane-1-carboxylate, sulfosuccinimidyl-2-[m-azido-o-nitrobenzamido]-ethyl-1,3'-dithiopropionate, dimethyl-3,3'-dithiobispropionimide-dihydrochloride and 3,3'-dithiobis[sulfosuccinimidylpropionate].
15. (canceled)
16. (previously presented) The carrier system according to claim 1, wherein said protein-based nanoparticles are based on human serum albumin.
17. (withdrawn) The method according to claim 7, wherein said functional proteins are avidin.
18. (withdrawn) The method according to claim 8, wherein the protein base is human serum albumin.

19. (previously presented) The carrier system according to claim 1, wherein said stable avidin-biotin complex is formed by incubation at 10°C.

20. (previously presented) The carrier system according to claim 1, wherein the nanoparticles, after forming said stable avidin-biotin complex, are purified by centrifugation and redispersion.

21. (previously presented) The carrier system according to claim 1, wherein the avidin which is covalently bound to the nanoparticles has 2,4 binding sites that are functionally available for forming said stable avidin-biotin complex.